
Tgfb1 expressed in the Tgfb3 locus partially rescues the cleft palate phenotype of Tgfb3 null mutants.

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Public Summary:

Although TGF-beta isoforms (TGF-beta1-3) display very similar biochemical characteristics in vitro, it has been determined that they demonstrate different or even opposing effects in vivo. During embryogenesis, TGF-betas play important roles in several developmental processes. Tgfb3 is strongly expressed in the prefusion palatal epithelium, and mice lacking Tgfb3 display a cleft of the secondary palate. To test whether the effect of TGF-beta3 in palatogenesis is isoform-specific in vivo, we generated a knockin mouse by replacing the coding region of exon1 in the Tgfb3 gene with the full-length Tgfb1 cDNA, which resulted in the expression of Tgfb1 in the Tgfb3 expressing domain. The homozygote knockin mice display a complete fusion at the mid-portion of the secondary palate, while the most anterior and posterior regions fail to fuse appropriately indicating that in vivo replacement of TGF-beta3 with TGF-beta1 can only partially correct the epithelial fusion defect of Tgfb3 knockout embryos. Palatal shelves of Tgfb1 knockin homozygote mice adhere, intercalate, and form characteristic epithelial triangles. However, decreased apoptosis in the midline epithelium, slower breakdown of the basement membrane and a general delay in epithelial fusion were observed when compared to control littermates. These results demonstrate an isoform-specific role for TGF-beta3 in the palatal epithelium during palate formation, which cannot be fully substituted with TGF-beta1.

Scientific Abstract:

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